Towards a standard MRI protocol for multiple sclerosis across the UK

Commentary

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Abstract

Multiple sclerosis (MS) is a chronic inflammatory demyelinating and degenerative disease of the central nervous system. It is the most common non-traumatic cause of chronic disability in young adults. An early and accurate diagnosis, and effective disease modifying treatment (DMT) are key elements of optimum care for people with MS (pwMS).

Magnetic resonance imaging (MRI) has become a critical tool to confirm the presence of dissemination in space and time of lesions characteristic of inflammatory demyelination, a cornerstone of MS diagnosis, over and above exclusion of numerous differential diagnoses. In the modern era of early and highly effective DMT, follow-up of pwMS also relies heavily on MRI, to both confirm efficacy and for pharmacovigilance.

Since criteria for MS rely heavily on MRI, an agreed standardized acquisition and reporting protocol enabling efficient and equitable application across the UK is desirable. Following a recent meeting of MS experts in London (UK), we make recommendations for a standardized UK MRI protocol that captures the diagnostic phase as well as monitoring for safety and treatment efficacy once the diagnosis is established. Our views take into account issues arising from the (repeated) use of contrast agents as well as the advent of (semi-) automated tools to further optimise disease monitoring in pwMS.

Commentary

Multiple sclerosis (MS) is an inflammatory demyelinating and degenerative disease of the central nervous system, and the most common non-traumatic cause of chronic disability in young adults (1). MS affects over 120,000 people in the UK (2). Early and accurate diagnosis, and effective disease modifying treatment (DMT) are key elements of optimum care for people with MS (pwMS) (3,4).

Ever since an International Panel chaired by the late Ian McDonald recommended its eponymous criteria for the diagnosis of MS, magnetic resonance imaging (MRI) has become a critical tool to confirm the presence of dissemination in space and time of lesions characteristic of inflammatory demyelination, cornerstones of MS, and to exclude numerous differential diagnoses (5). In the modern era of early and highly effective DMT, follow-up of pwMS also relies heavily on MRI, for disease control and pharmacovigilance.

Since MRI criteria for MS are based on specific techniques, agreed standardized acquisition and reporting protocols across the UK are desirable. This will facilitate continued monitoring of pwMS moving to different parts of the country. In the longer term, it also will provide comparable imaging and outcomes data that, when considered together, could inform better clinical decision-making. To discover whether any de facto standardisation already is in place – despite the lack of formal agreement – we undertook a brief survey among neuroradiology trainees. A link to the survey, open between 2nd of January and 30th of March 2018, was sent out twice using the email database of the British Society for Neuroradiologists trainee list. Ten trainees from eight centres (Bristol, Cambridge, Leeds, Manchester, Newcastle, Norwich and two in London) responded. Heterogeneity of scanning protocols for MS among institutions was evident: only 50% acquired any volumetric sequences, and there was no consensus on the non-volumetric FLAIR, with coronal, sagittal and axial planes used in different centres. Of note, only a single centre used gadolinium contrast by default in all (diagnostic and follow-up) investigations of pwMS. The remainder of the centres restricted routine use of contrast administration to diagnostic scans. MRI measures of disease burden and its progression thus are not comparable across UK centres. Albeit based on a limited sample, this illustrates the need for standardisation.

Whilst the diagnostic principles for MS have recently undergone their third revision (6), there has perhaps been lesser emphasis on acquisition techniques. However, to provide an equitable service across the country within the financial constraints of the NHS (7), an efficient way to enable best practice in MS that covers the diagnostic and follow-up/monitoring phases is warranted. There is no need to “reinvent the wheel”, since both the Magnetic Resonance Imaging in MS (MAGNIMS) (8) and the Consortium of MS Centres (CMSC) (9) networks have recently updated their evidence-based guidance on MRI in MS. Detailed suggestions provided by a Swedish consensus statement provide further reference points for a UK protocol covering the techniques used, timelines for scanning, as well as requesting and reporting guidelines (10) (Table 1). However, while there are communalities among these protocols, most of them are too long (and partially redundant) to be used efficiently in the NHS. There is a need to develop a more concise, cost effective protocol for the UK which will balance the cost of scanning time and the information provided.

A cornerstone of most recommended brain protocols is 3D rather than 2D FLAIR to (i) improve sensitivity for lesion detection and (ii) enable reconstruction in any desired plane thereby mitigating differences in the longitudinal assessment due to imperfect scanning plane alignment and patient repositioning. On modern scanners, such 3D-FLAIR sequences can now be obtained in under 5 minutes. The general advantage of using 3D sequences is that longitudinal scans can be registered and subtracted, which greatly facilitates detection of new lesions and improves inter-observer variability (11)

Detection of disease activity through new FLAIR lesions may also reduce the need to use gadolinium, which carries the risk of deposition in the CNS.

Recently, several (semi-)automated tools to estimate MS lesion changes as well as whole brain and white/grey matter volumes have been CE marked and some have been FDA approved (12). These new technologies are designed to not only assist the radiologist in the detection of lesions, but also to quantify volume changes. Evidence suggests that using these tools to guide radiologists may reduce both inter-observer variability and reading time (13). Moreover, brain volume changes can be reliably quantified in ways that may contribute to clinical decisions. While the data is not yet available to evaluate the utility of these measures in clinical practice and current expert guidelines thus do not recommend their routine use (8), it would be prudent to consider these and other emerging analytical technologies for clinical decision support when formulating a UK protocol.

With highly active DMT focussing on the adaptive immune response, characteristic risk profiles have emerged that warrant use of specific methods for MRI monitoring. The major example of this is monitoring for the risk of progressive multifocal leukoencephalopathy (PML) due to the long term treatment of pwMS with natalizumab (Tysabri) and - rarely - other DMTs for pwMS (14). Other DMT-associated opportunistic infections also are being recognized (15). As highly active DMT use become commonplace across the country, mitigation of the risks by frequent (3-6 monthly) MRI monitoring is needed, for which an abbreviated protocol including only 3D-FLAIR, 2D-T_2 and DWI is recommended (https://ms-pml.org/).

Since markers of MS disease activity based on biofluids are only slowly emerging, the quality of both diagnostic as well as follow-up MRI will, for the time being, remain key for the optimum care of pwMS. This has most recently been recognized by a dedicated satellite panel at the annual meeting of the Association of British Neurologists in April 2018. We encourage the neuroradiology community in the UK to take the next step and develop a nationwide efficient protocol that enables best care as well as equity in the diagnosis and follow-up of pwMS across the NHS.

Table 1: Recommended MRI protocols for diagnosis and follow-up of people with multiple sclerosis adapted from references 8–10 (acquisition times).

Consortium of Multiple Sclerosis Centres Task Force

Core sequences	Optional sequences
Anatomic 3D inversion recovery (IR) T_1 gradient echo attenuation (5:21)	Axial proton attenuation
Gadolinium single dose (0.1 mmol/kg for 30 seconds) 2D (3:20)	Pre- or post-gadolinium axial T_1 spin-echo (for chronic black holes) (3:20)
3D sagittal T_2 weighted image (WI) FLAIR within T2 lesions	SWI for identification of CVS (3:02)
3D T_2WI b	
2D axial diffusion weighted imaging (DWI) (5-mm sections, no gap) (1:52)	
3D FLASH (non-IR prepared) post-gadolinium	
3D series (eg 1.0-1.5mm thickness); typically reconstructed to 3mm for display and comparison of lesion counts	

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Diagnostic	Follow-up
3D T_1 (Pre-contrast) (5:21)	Gadolinium-based contrast agents
Haemorrhage sensitive sequence (SWI, gradient recalled echo or fast field echo) (3:02)	Axial T_2 (2:20)
DWI (1:52)	3D T_2 FLAIR (5:42)
Gadolinium-based contrast agents	3D post-gadolinium T_1 (5:21)
Axial T_2 (2:20)	
3D T_2-FLAIR (5:42)	
3D T_1 (post-gadolinium) (5:21)	

MAGNIMS Standardized MRI Protocol

Brain – diagnostic	Follow-up
Axial 2D PD or T_2-FLAIR (2:44)	Axial 2D PD (2:20) or T_2-FLAIR (2:44)
Axial 2D T_2-weighted (2:20)	Axial 2D T_2-weighted (2:20)
Sagittal T_2-FLAIR 2D (2:44) or 3D (5:42)	Contrast-enhanced T_1-weighted 2D (3:20) or 3D (5:21)
Contrast-enhanced T_1-weighted 2D (3:20) or 3D (5:21)	

Spinal cord – diagnostic

Sagittal 2D PD*/T_2-weighted sequences (3:36)
Sagittal 2D contrast-enhanced T_1-weighted (2:00)
*STIR can be used alternatively
Optional: axial 2D T_2-weighed sequences

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Aaxial 2D T_2-weighted (2:20)	Aaxial 2D T_2-weighted (2:20)
Ssagittal T_2-FLAIR 2D (2:44) or 3D (5:42)	Ccontrast-enhanced T_1-weighted 2D (3:20) or 3D (5:21)
Contrast-enhanced T_1-weighted 2D (3:20) or 3D (5:21)	

Spinal cord – diagnostic

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Sagittal 2D contrast-enhanced T_1-weighted (2:00)
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